Is there a case for MDMA-assisted psychotherapy in the UK?

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Is there a case for MDMA-assisted psychotherapy in the UK?

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Abstract

Much has been written in scientific and popular literature in recent years about the dangers surrounding the recreational use of the drug MDMA/ecstasy.

What is little known and understood however is the history of the apparently safe and effective use of MDMA as a therapeutic tool for psychotherapy. In this paper the author explores this history and describes the recent re-emergence of scientific interest in MDMA and other psychedelic drugs. There are currently several new double-blind randomised controlled trials underway re-visiting the subject. By acknowledging the limitations of this new research and emphasising the importance of exercising appropriate but realistic caution, the author asks that the medical profession consider a dispassionate and open-minded debate to examine whether MDMA might have a legitimate place as an adjunct to psychotherapy in modern psychiatric practice.

Key words

MDMA, ecstasy, psychedelic drugs, psychotherapy

What is MDMA?

MDMA (3,4-methylenedioxmethamphetamine) is the synthetic psychoactive drug better known as the street drug 'ecstasy'.

First patented in 1912 by E. Merck in Germany, it was briefly researched using animal experiments by the American Army Chemical Centre as a potential brainwashing agent in 1953 (Holland, 2001a). Then, in the 1960s an analogue of MDMA, the longer-acting MDA, became used as a recreational drug. The subsequent massive recreational use of MDMA since the 1980s is well documented.

What is less well known is the use of MDMA by psychotherapists before it was made illegal. In this paper I will describe the characteristics of the MDMA experience that make it a potentially useful drug for therapy, briefly explore the history of other psychedelic drugs in therapy, look at the risks associated with the use of MDMA and then outline the state of contemporary MDMA psychotherapeutic research.

Characteristics of the experience

The MDMA experience has several features that make it well suited to assist psychotherapy. Sometimes referred to as an 'empathogen' or 'entactogen', MDMA promotes relaxation, facilitates a loosening of the ego and encourages an increased thoughtfulness and contemplativeness (Vollenweider *et al*., 1998). These effects can produce a state of improved insight and aid a greater exploration of otherwise painful repressed memories, by 'inhibiting the subjective fear response to an emotional threat' (Greer and Tolbert, 1998).

This makes MDMA a particularly useful drug for patients with PTSD (Bouso, 2001) or for patients experiencing anxiety associated with the process of dying in cases of terminal cancer (Greer and Tolbert 1990).

There are also well-recognized effects on the *relationship* between the patient and the therapist. These stem from MDMA's ability to increase levels of understanding and closeness. These empathogenic effects are well documented (Liester *et al*., 1992; Cami *et al*., 2000; Sumnall *et al*., 2006). The warmth and feelings of empathy that are experienced under MDMA allow users to approach previously difficult intimate relationship conflicts in a new light, and account for the utilization of MDMA as an agent to assist in couples therapy in the United States in the early 1980s (Greer and Tolbert 1986).

The history of psychedelic psychotherapy

After the discovery of the psychotropic effects of LSD in the 1940s by the Swiss chemist Albert Hofmann (Hofmann, 1980), there followed a short-lived period of clinical use within psychiatry. Psychiatrists found LSD had the ability to allow a deeper access to repressed memories and an improved relationship

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between patient and therapist. The 'classical' psychedelics such as LSD and psilocybin were studied throughout the 1950s and 1960s, and thousands of case reports of their safe use exist (Masters and Houston, 1970). The number of adverse incidents was low and doctors developed progressively sophisticated methods for achieving the most comfortable and productive psychedelic sessions. Their techniques were often informed by Eastern tradition – with elements of meditation and chanted verses in a relaxing, facilitative environment (Grof, 1980). However, despite these numerous reports, by modern research standards the studies of the 1950s and 1960s have little more than anecdotal value as they usually lacked control groups and follow-up and were subject to selection bias (Grob, 1994).

With the leaking of LSD from the scientific community into widespread public use, the medical research was ended virtually overnight as doctors, in the face of a massive press bias against LSD, were forced to distance themselves from the drug (Sessa, 2005). Many psychedelic therapists, having found their work with LSD promising, were disheartened by the prohibition.

It was not until 10 years later that MDMA began to be explored as an adjunct to psychotherapy. MDMA – which is not, strictly speaking, a 'classical' psychedelic drug – offered several advantages. Not only was it shorter-acting than LSD, but also it crucially lacked some of the more intense perceptual and identity distortions of the LSD experience. Indeed, the MDMA experience was almost invariably positive in any user. This made it a more manageable tool in the clinical context.

The development of MDMA as a clinical tool in the 1970s and 1980s

The emergence of MDMA as an agent for psychotherapy can be significantly attributed to the pioneering work of Dr Leo Zeff, from California. Zeff had been a psychedelic psychotherapist during the 1960s using LSD. By the early 1970s he had ceased this work, but on discovering the psychoactive effects of MDMA, he came out of retirement and continued therapy with this new drug. It is estimated that, by the time of his death in his seventies, he had introduced (the then still-legal) MDMA to over 4000 patients. Many of those who received psychedelic therapy under him went on to become therapists themselves (Holland, 2001).

Largely based in and around California, from the mid-1970s to the mid-1980s, there was a growth of clinicians using MDMA (then known as 'Adam'). Few published research trials exist of its use by therapists – and none that have the quality of double-blind placebo control – but there are many accounts of successful case reports and informal therapy outcome studies (Stolaroff, 2004).

A paper by psychiatrist George Greer describes the therapeutic methods and the subjective reports of 29 patients who were administered MDMA as part of individual, group and couples therapy in the early 1980s (Greer and Tolbert, 1986). There were no significant physical complications from taking the drug, and the overwhelming majority of subjects reported positive individual effects, improved well-being and the resolution of relationship problems after their therapy. In a later review of 80 patients who received MDMA therapy between 1980 and 1985, Greer outlined the careful methods and experimental techniques that facilitate a successful drug-assisted session. He also acknowledged the limitations of these studies, and suggested that further, controlled studies occur (Greer and Tolbert, 1998). However, the almost total prohibition of all MDMA clinical research that has occurred since 1985 has prevented such studies until very recently.

Recreational use and the scheduling of MDMA

Since the 1980s the shift of MDMA from the legitimate medical context to its use by a wider public has not been dissimilar to that of LSD. MDMA leaked from the medical community and became the drug of choice for young people attending the rave/dance music scene. By the mid-1980s, there were increasing negative reports of its uncontrolled use outside of the clinical environment, and despite little evidence of harm, the American Drug Enforcement Agency (DEA) called for the drug to be banned.

Those clinicians who had been using the drug safely and effectively for 10 years requested that the case for medical applications for MDMA be heard – so at least the scheduling would reflect the calls for further clinical research to take place. This request was disregarded and the DEA used emergency measures to bypass a hearing and make the drug a Schedule One controlled substance in the USA in 1985. This labelled MDMA as having a high risk of addictive abuse potential and no evidence of medical applications. Therapists were forced to give up using MDMA, and the research collapsed overnight.

In the UK, the 1971 Misuse of Drugs Act (which had already been altered in 1977 to include all ring-substituted amphetamines such as MDMA, MDA, MDE etc.) was further amended in 1985 to refer specifically to ecstasy – placing it in the Class A category (Holland, 2001b).

There then followed a growth of government-sponsored scientific studies exploring the dangers of MDMA. These frequently involved giving animals extremely high doses of MDMA over prolonged periods. Some studies suggested heavy, recreational ecstasy use might be linked to neurotoxicity (Molliver *et al*., 1990), particularly when the drug is taken frequently and in high doses (Ricaurte *et al*., 1985).

The risks associated with MDMA

The debate about the potential neurotoxicity of MDMA in humans continues. The prohibition on studying the drug on human subjects restricts researchers to conducting their studies on either selectively biased populations of recreational ecstasy users (who frequently use other drugs or alcohol, or have pre-existing mental-health problems) or on animal models that translate poorly to humans.

Many recreational ecstasy users take several tablets every weekend – together with other drugs, particularly cannabis and alcohol, but also frequently amphetamines and cocaine (Sherlock and Conner, 1999).

Therefore, studies describing the dangers of recreational ecstasy consumption refer to doses or patterns of use that are irrelevant to those proposed for MDMA psychotherapy (Sessa *et al*., 2006).

The dose of MDMA given in the clinical context (for instance, those described in the contemporary studies below or in the past studies of the 1980s outlined by George Greer) is usually a standardized 75–125 mg, sometimes with a second booster dose of 50 mg given several hours into the session. The contemporary studies then describe a gap of about 4 weeks before another drug session occurs.

The studies conducted as part of the Phase One trials for the current MDMA psychotherapy projects underway have demonstrated that, when given in limited, infrequent and moderate doses (as in the psychotherapeutic setting), the drug has no lasting neuropsychological or neurocognitive effects (Halpern *et al*., 2004) and no evidence of neurotoxicity (Ludewig *et al*., (2003).

Factors that may influence risk

Like LSD, when MDMA is taken without attention paid to set and setting, it has potential to cause harm. In the UK, in the 10 years since 1994, there have been 165 deaths attributed solely to ecstasy (Schifano *et al*., 2006). This figure is remarkably small, given that there are at least 100 million tablets of ecstasy (containing varying quality preparations of MDMA plus any other drug) distributed in the UK each year (National Criminal Intelligence Service, 2001). By contrast, *annually*, there are around 7000 alcohol-related deaths (several thousand of which relate to acute intoxication) and 106 000 tobacco-related deaths (Office of National Statistics, 2003).

Some users most likely have a genetic predisposition to the potential harmful physical and psychological effects of MDMA, which then interact with certain environmental factors (Soar, 2006). There are two major ways in which recreational ecstasy users can suffer acute toxicity.

The first is through hyperthermia. This may occur through prolonged physical exertion in a hot environment, combined with dehydration secondary to not consuming enough water. The euphoric effects of the drug may lead to the user failing to notice the usual thermostatic cues and continuing to dance vigorously despite the rising temperature. The sequalae of hyperthermia include liver and kidney failure and cerebral oedema. Further serious complications include rhabdomyolysis and disseminated intravascular coagulation (Nimmo *et al*., 1993). High temperature has also been demonstrated to further exacerbate the risk of longer-term neurotoxicity (Malberg and Seiden, 1998).

The second cause of acute toxicity is ecstasy-induced hyponatreamia. In vulnerable individuals with a genetic predisposition for the condition, MDMA can cause an impairment of the kidney's normal water homeostasis mechanism via an increase in arginine vasopressin (ADH) that can lead to excess water retention (Wolff *et al*., 2006). When this is combined with potential for excessive water consumption (as has sometimes occurred because users have been over-vigilant about the risks associated with dehydration), there can be associated decreased serum sodium, which in turn leads to nausea, weakness, fatigue, confusion, seizures and coma.

So, in summary, when ecstasy is taken in uncontrolled circumstances, in extreme heat and with vigorous exercise, there may be problems associated with either drinking *too much* or *too little* water.

Of course, physical factors such as temperature, exercise and water consumption can easily be controlled in a clinical setting. This has been demonstrated by the Phase One trials for the contemporary MDMA psychotherapy studies. They did not record any significant changes in temperature in the human subjects and no associated abnormal water homeostasis reactions occurred (www.maps.org/research/mdma/ptsd_study/protocol) – further illustrating that severe toxicity reactions associated with uncontrolled recreational ecstasy use do not analogize at all accurately to proposed clinical applications with MDMA.

More recent clinical research with MDMA

There was a brief resumption of MDMA therapy in Switzerland between 1988 and 1993. Permission was granted for three psychotherapists from the Swiss Medical Society for Psycholytic Psychotherapy to use MDMA and LSD as part of on-going treatment for their patients.

Patients were given the drugs in low-to-moderate doses, and therapy was conducted both individually and in groups. The patients had diagnoses of personality disorders, affective disorders and adjustment disorders – many with co-morbid addiction problems.

In a follow-up study, 171 patients were asked for their subjective retrospective experiences of the therapy (Gasser, 1995). The majority of patients reported an improvement in function and well-being and a reduction in the use of substances.

Current studies

After a hiatus of almost 40 years, there are now two new psychedelic drug research projects underway (one with MDMA and one with psilocybin), and several more MDMA projects in the final stages of planning.

In South Carolina, USA, the psychiatrist Dr Michael Mithoefer is currently running a double-blind trial comparing MDMA-assisted psychotherapy with a placebo in the treatment of Post Traumatic Stress Disorder. The treatment consists of two sessions of MDMA-assisted therapy interspersed with non-drug sessions. There are baseline, outcome and follow-up evaluations using standard psychiatric rating scales. Dr Mithoefer's hypothesises that the MDMA group will show a significant and lasting reduction in symptoms. He further proposes there will be no evidence of neuropsychological or neurocognitive deficits. Similar projects using MDMA to treat PTSD are due to start in Spain, Switzerland and Israel later this year.

Another double-blind placebo-controlled study involving MDMA that is not yet started but soon to be underway is being

run by Dr Halpern of Harvard Medical School. The subjects are men and women diagnosed with advanced-stage cancer, with 12 months or less of expected remaining life, who are experiencing diagnosis-associated anxiety. Again, subjects receive just two drug-assisted sessions alongside a course of non-drug psychotherapy. The hypotheses are that the MDMA group will experience significant dose-dependent decreases in anxiety and usage of analgesic and anxiolytic medication after each experimental session and at 2 months' follow up. Dr Halpern also hypothesises that there will be dose-dependent improvements in quality of life.

Already underway is a similar project, being run by Dr Charles Grob of UCLA. Like Dr Halpern, Dr Grob is looking at the therapeutic application of psychedelics for terminal cancer sufferers, using the drug psilocybin (the active component in magic mushrooms) rather than MDMA.

All of these projects have taken years to gain regulatory and ethical approval. The details for these studies can be found at the websites for the Multidisciplinary Association for Psychedelic Studies (www.maps.org) and the Heffter Research Institute (www.heffter.org).

Do we really need MDMA-assisted psychotherapy?

The western world is facing a growing epidemic of mental health problems (WHO, 2003). Despite guidelines recommending a broad range of treatment approaches, stressed and under-resourced doctors are increasingly relying on pharmacological treatments alone, and over-prescribing drugs in an effort to manage their growing numbers of patients (Pomerantz, 2003). Whilst there are also progressively more sophisticated models of psychotherapy that offer brief, time-limited and cost-efficient therapies such as Cognitive Behavioural Therapy, Dialectical Behavioural Therapy and Inter-Personal Therapy, even these streamlined models of psychotherapy are time-consuming and expensive.

The reports of the 1950s and 1960s with LSD and the reports from the 1980s using MDMA suggest combining traditional methods of psychotherapy with drugs appears to quicken and deepen the experience of therapy. The current studies underway in the United States use only infrequent doses of the drug, combined with non-drug sessions as part of a structured and time-limited course of problem-focused psychotherapy. There are reports from the last 40 years describing how these drugs can offer a breakthrough for sufferers with chronic mental illness that had previously been resistant to other treatment methods with drugs or traditional therapy (Grinspoon and Bakalar, 1998). If it could be the case that drug-assisted psychotherapy can accelerate an otherwise slow and expensive process, this would have good implications for a health-care system already buckling under strain.

Summary

Despite the potential therapeutic promises and low safety risks of MDMA-assisted psychotherapy, one must take care to remain objective. The subject of psychedelic psychotherapy in the past collapsed – in part – because it was not only the pop-stars and poets who were preaching about the wonders of LSD, but also some clinicians allowed themselves to become biased and blinded to the potential dangers of the drug.

We are right to remain sceptical about a new therapy that, in the eyes of the general public, is associated with recreational drug abuse. MDMA, when used irresponsibly, has certainly been shown to cause physical, psychological and social harm, and even deaths. So we must be cautious and not disregard the concerns of those people who fear that medical use of MDMA may cause greater social and health problems than it may solve.

Nevertheless, despite the fact that some people abuse MDMA and come to harm through this, can we as doctors ignore the emerging research suggesting MDMA may have positive applications for modern psychiatry?

To view this new research objectively would mean seeing beyond the prejudices associated with uncontrolled recreational drug abuse and focusing dispassionately on the realistic risk–benefit ratio when MDMA is used in the clinical setting. As Dr Mithoefer puts it, in the protocol for his on-going MDMA-assisted psychotherapy treatment for PTSD study: The possibility of developing a novel means of reducing or alleviating symptoms in treatment-refractory posttraumatic stress disorder outweigh the low risks of administering two 125 mg doses of MDMA in a controlled laboratory setting. Michael Mithoefer, January 2005, www.maps.org/research/mdma/ptsd_study/protocol.

We are of course only at the very earliest stage of this new development, but we have enough evidence from the MDMA psychotherapy studies of the past to at least power further research into the drug. Then we can establish whether those promising early results will truly stand up to modern double-blind RCT research conditions. But we certainly ought not be put off by the fact that earlier trials were merely anecdotal. After all, many medical trials often begin only at the level of promising anecdotal evidence.

The continued scheduling of MDMA as a substance with high abuse potential and no medical uses is increasingly under attack by scientists working within the fields of medicine, neuroscience, psychopharmacology and even philosophy, who are noticing the benefits for increasing the scope of work with this substance (Nutt, 2006). The evidence against *at least researching* MDMA for psychotherapy appears to be very scant indeed.

Nevertheless, there are no clinical trials underway, or even under discussion, in the UK at present. Given the problems faced by researchers in the States to get their contemporary MDMA research off the ground, it is certain that it will take a brave, committed and politically astute clinician to propose this kind of research here. But if this contentious drug really can be employed safely and effectively in the treatment of resistant mental illness, perhaps there could be a case for MDMA-assisted psychotherapy in the UK.

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Disclaimer

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